Palliation of Abdominal Aortic Aneurysms in the Endovascular Era

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WHAT THIS PAPER ADDS?
There have been a few papers that have dealt with the issue of palliation of patients diagnosed with an abdominal aortic aneurysm who are not fit for operative repair, but none that consider this issue alongside the use of CPEX testing. This topic is one that will be increasingly pertinent in the era of outcome reporting.

Objectives: To establish outcome of patients with abdominal aortic aneurysm (AAA) deemed unfit for repair.
Design: Retrospective non-randomised study.
Materials and methods: Identification of males with >5.5 cm or females with >5.0 cm AAA turned down for elective repair between 01/01/2006—24/07/2009 from a prospective database. Comorbidities, reasons for non-intervention, aneurysm size, survival, use of CPEX (cardio-pulmonary exercise) testing and cause of death were analysed. Although well-established at the time, patients unfit for open operation were not considered for endovascular repair.
Results: Seventy two patients were unsuitable for AAA repair. Aneurysm size ranged from 5.3 cm to 12 cm. Functional status, comorbidity and patient preference determined decision to palliate. Sixty percent of patients were alive at study close. Aneurysm rupture was cause of death in 46%. CPEX testing was performed in 54%, whose mortality was 28%, vs. 54% in the non-CPEX group ($P < 0.05$).
Median survival of patients with 5.1—6.0 cm AAA was 44 months and 11% died of rupture. Between 6.1 and 7.0 cm median survival was 26 months and 20% died of rupture. However, with >7 cm aneurysms, survival was 6 months and 43% ruptured.
Conclusion: Under half the deaths in our comorbid cohort were due to rupture. However, decision to palliate may be revisited as risk-benefit ratio changes with aneurysm expansion.

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INTRODUCTION

Increasing use of medical imaging and the introduction of a national screening programme will increase the number of patients with abdominal aortic aneurysms referred to vascular surgeons in the UK. Even once at a size that mandates consideration of repair, there will always be some patients in whom the risk of aneurysm repair will outweigh potential survival benefits and those in whom the likelihood of death from non-aneurysm-related causes is greater than that from the aneurysm itself. In these cases, life expectancy would not increase despite intervention and the significant mortality and morbidity this entails. This holds true despite the widespread introduction of minimally invasive endovascular techniques, which may be favoured in less fit patients should the anatomy allow, but whose survival is not improved following intervention.[1] Several studies have looked at long-term outcomes in this cohort, dating back to Szilagyi in the 1970s.[2]

Patient selection for aneurysm surgery (whether endoluminal or open) is based on a number of factors, including Consultant Vascular Surgeon assessment, cardio-pulmonary exercise testing (CPEX) and Consultant Anaesthetist review. The aim was to establish outcome of patients diagnosed with an abdominal aortic aneurysm (AAA) deemed unfit for surgical intervention and determine whether this selection process is justified.

MATERIALS AND METHODS

Our unit is a district general hospital serving a resident population of almost 300,000, with a high proportion of elderly patients. Selection of patients suitable for aneurysm repair is based on initial assessment in the outpatient clinic by a Consultant Vascular Surgeon. This takes into account comorbidities and functional status, as well as aneurysm anatomy.

Patients referred with an ASA grade of 4 or above are excluded based on poor physiological reserve to withstand operative stress. Some of these patients subsequently

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undergo CPEX testing on patient request. Those with an ASA grade <4 are then referred to a Consultant Anaesthetist for further assessment +/− CPEX testing and depending on results and patient choice a management decision is made.

Endovascular aneurysm repair (EVAR) techniques have been used in our unit since 2005 but were performed by our consultants at a different centre, prior to this. EVAR was therefore well-established by the study period. However, following recommendations from the EVAR-2 trial,[1] comorbid patients with poor physiological reserve were not considered for endovascular repair, even if amenable.

In our unit, a prospective database of patients diagnosed with an AAA referred from outpatient and inpatient sources is maintained. After 2000, patients from an aneurysm screening programme were included. Using this database, males with a >5.5 cm AAA or females with a >5.0 cm AAA (as defined by the UK small aneurysm trial[3]), turned down for elective open aneurysm repair between 01/01/2006—31/07/2009, were retrospectively identified. Patients who initially presented with ruptured, suprarenal or thoracic aneurysms were excluded.

Aneurysm size was defined as maximum diameter on ultrasound or, where not available, CT scanning. Aneurysm size at the time of decision to palliate was confirmed by reviewing images on our online radiology system. Hospital records were obtained for all patients and reasons for non-intervention determined. Cause and time of death were confirmed by examining death certificates for those who died in hospital, by analysing post-mortem reports where applicable or by consulting the local Public Health Department for those who died in the community.

Cardio-pulmonary exercise (CPEX) testing began in our unit in 2002. Following a diagnosis of a large abdominal aortic aneurysm, patients are subjected to physical cardio-pulmonary stress on an exercise bike in order to determine fitness for surgery. Anaerobic threshold (AT) (the oxygen consumption level during exercise at which aerobic respiration is substituted by anaerobic mechanisms) and VO_2 max (maximum oxygen consumption during exercise or aerobic capacity) among other parameters are then measured and the readings obtained used to determine an objective prediction of likely physiological outcome after surgical stress. This predicted mortality, combined with clinical judgement, is used to decide whether a patient should go forward for surgery and has been demonstrated to be an accurate predictor of survival.[4,5] Use of CPEX testing for each individual in our study and readings for anaerobic threshold and/or VO_2 max were recorded where applicable. Values for VO_2 max were not available in all cases as, on introduction of CPEX testing, this parameter was not universally determined.

Comorbidities, reasons for non-intervention, aneurysm size, survival, use of CPEX testing and cause of death were recorded and results analysed. Survival was calculated from the date of decision to palliate, with end-points being death or close of study. Patients alive at the end of the study were censored to the non-rupture group. Survival curves were plotted using Kaplan—Meier analysis, with comparison using the log rank test. For categorical data, differences between groups were compared using the Fisher's exact test. Medcalc statistical software (version 12.0.3.0) was used to perform statistical analysis and a P value <0.05 was taken to indicate significance.

RESULTS

A total of 72 patients were palliated during the study period (55 men and 17 women; ratio 3.2:1). Mean age was 80 years (range 58—93, SD 7.6).

Over a similar period, 122 non-ruptured AAA repairs and 39 ruptured AAA repairs were performed in our unit. 66% (81 patients) of elective repairs and 5% (2 patients) of emergency repairs were performed using EVAR techniques. Mean age in the non-ruptured aneurysm repair group was 71 (range 56—86) and in the ruptured group was 77 (range 60—94). 30-day mortality for non-ruptured and ruptured aneurysm repairs were 2.46% and 30.76% respectively. Thus, a total of 194 patients presented in the study period with non-ruptured AAA of whom 72 (37%) were initially not offered surgical repair.

Reasons for non-intervention are shown in Table 1. No patients were turned down on grounds of old age alone, other factors such as comorbidity and functional status also being taken into account. Distribution of ASA grade within our cohort, percentage mortality and percentage rupture according to ASA grade can be seen in Fig. 1. The majority of patients with an ASA score of 2 declined operative intervention (5/7 patients).

Overall, 60% (43/72) of patients were alive at end of the study. Overall whole group median survival was 34 months with a 5 year survival of 4.2%.

Male mortality was 45% and female 24%. Cause of death is shown in Table 1. The commonest cause of death was aneurysm rupture, 41% ($n = 12$). However, patients dying of ruptured AAA had a significantly longer survival period (median 11 months, range 0.4—75 months) compared to non-aneurysm related deaths (5 months, range 2.6—26 months), $P = 0.04$ (Fig. 2). We were unable to determine cause of death in 1 patient, as he died abroad.

Only 7 (24%) of our patient group underwent post-mortem examination and of these, 4 died of a ruptured aneurysm. Cause of death was determined from death certificates in a further 13 patients. In the remaining cases, the local Public Health Department was consulted.

Ten patients refused surgery (mean age 80 vs. 81 for all other patients). Of this group, 4 died before the end of the study, 3 of these due to aneurysm rupture. The fourth died from a myocardial infarction (Fig. 3: Summary of outcomes for patient cohort). Survival in the patient refusal group was greater than that in the group of patients turned down on clinical grounds, (although statistical significance was not reached); median survival in the patient refusal group being 46 months compared with 26 months for those turned down for repair ($P = 0.08$).

Patients were stratified into 3 groups based on aneurysm size at the time of a decision to palliate in order to assess

Table 1. Reasons for non-intervention.

Reason for non-intervention	Number of patients	% Died	Cause of death
Patient refused	10	40% (4 patients)	3 Ruptured AAA
Cardiovascular disease	7	86% (6 patients)	2 Ruptured AAA 2 MI 1 Cardiorespiratory arrest 1 Renal failure
Chronic obstructive pulmonary disease	15	33% (5 patients)	3 Ruptured AAA 1 Sepsis 1 Unable to obtain
Carcinoma	7	43% (3 patients)	3 Carcinoma
Multifactorial: >2 of CVE, IHD, Cardiac failure, Carcinoma, COPD, poor CPEX result, DM, Chronic renal failure, Dementia	27	30% (8 patients)	2 Ruptured AAA 2 Sepsis 1 CVA 1 Renal failure 1 Respiratory arrest 1 Dementia
Poor exercise tolerance	5	40% (2 patients)	2 Ruptured AAA
Dialysis-dependent chronic renal failure	1 (aged 80)	100% (1 patient)	1 MI

the effect of AAA size on survival (Table 2 and Fig. 4). As would be expected, as aneurysm size increased so survival decreased significantly.

Four patients underwent AAA surgery after an initial decision not to proceed. Two patients underwent elective open aneurysm repair: 1 at another unit, following assessment by a different Vascular team (post-operative survival at the close of the study = 17 months) and 1 as the aneurysm size increased sufficiently to warrant the risks of surgery. Unfortunately, this patient died post-operatively. Two patients in our cohort, presenting with rupture, underwent emergency open aneurysm repair following further discussion with patient and family regarding decision to palliate. One of whom survived (post-operative survival at the close of the study = 3.5 months) and one of whom died following surgery at another centre.

On assessment of anatomical suitability for endovascular aneurysm repair, 58% (42 patients) were seen to be amenable to EVAR. Of these, 6/42 (14%) refused intervention and of those left, 3% (1 patient) were ASA-2, 53% (19 patients) ASA-3 and 44% (16 patients) ASA-4. In keeping with recommendations from the EVAR-2 trial,[1] if patients were deemed unfit for open aneurysm repair, they were not put forward for endograft repair.

Forty patients (56%) underwent CPEX testing. Mortality in this group was 28% compared with 55% in the non-CPEX group ($P < 0.05$) (median survival 46 vs. 21 months). Values for anaerobic threshold ranged from 4 to 14 mlO_2/kg/min but 6 patients were unable to pedal adequately to reach anaerobic threshold. VO_2 max varied from 5.6 ml/kg/min to 15.6 ml/kg/min but was not recorded for 11 patients, including 2 patients who were unable to perform the test

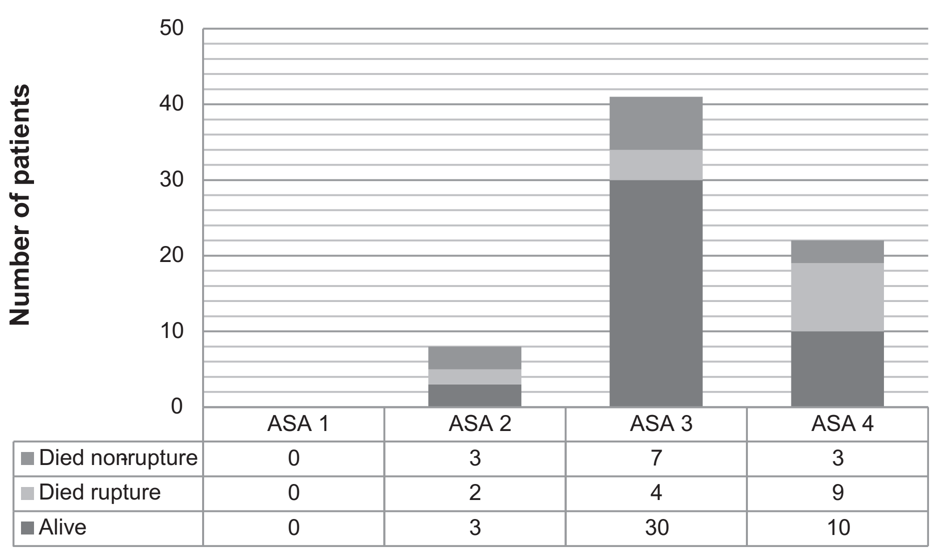
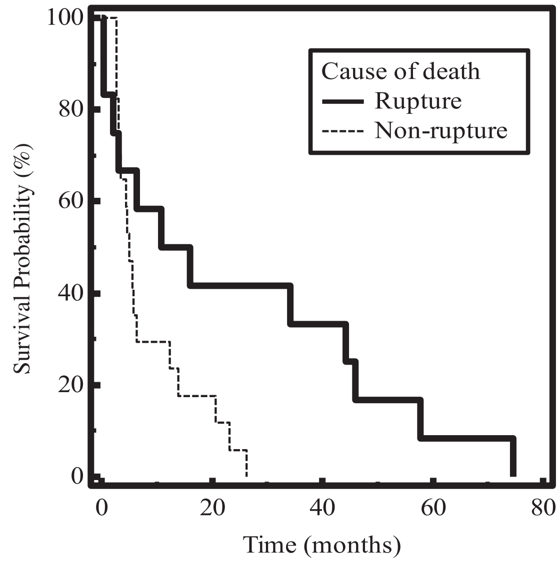


Figure 1. Graph to show patient outcome and cause of death when stratified according to ASA grade.



Number at risk:

Rupture	12	5	4	1	0
Non-rupture	16	3	0	0	0

Figure 2. Survival when stratified according to cause of death.

due to technical difficulty. This was very much in the early days of our CPEX programme.

DISCUSSION

The number of patients palliated by each surgical unit will depend on patient fitness and surgical thresholds for intervention. Over the study period, 37% of those presenting to our unit with non-ruptured AAA were initially conservatively treated.

This rate is slightly higher than that seen on literature review, quoted figures ranging from 18% (Heikkinen et al.[6]) to 32% (Szilagyi et al.[2]). However, half of the papers reviewed did not state volume of elective work and so palliation rates were not calculable.

The obvious question arises: are we being too exclusive in our selection policy for operative repair? Our elective mortality for AAA repair (open and EVAR) being 2.5%, compared with 4.2% from the 2009 National Vascular Database.[7] It is likely that this difference is largely attributable to our patient demographic, which consists of a high proportion of elderly and consequent high endemic co-morbidity, precluding aneurysm repair.

Our end-of-study survival (60%) is equivalent to that of the non-operated group in the EVAR-2 trial[1] and our rupture rate of 41% is similar to that quoted by Szilagyi (45%),[2] Lederle[8](40%) and Jones[9] (38%). Mortality rates in the literature ranging from 29%[10] to 49%[11] (See Table 3). Unsurprisingly, in keeping with the literature,[9,11] median survival declined and proportion of patients dying from rupture increased with increasing aneurysm size.

Darling[10] reviewed outcomes following emergency surgery in 60 consecutive patients presenting in the 1960s with aneurysm rupture who had been turned down for

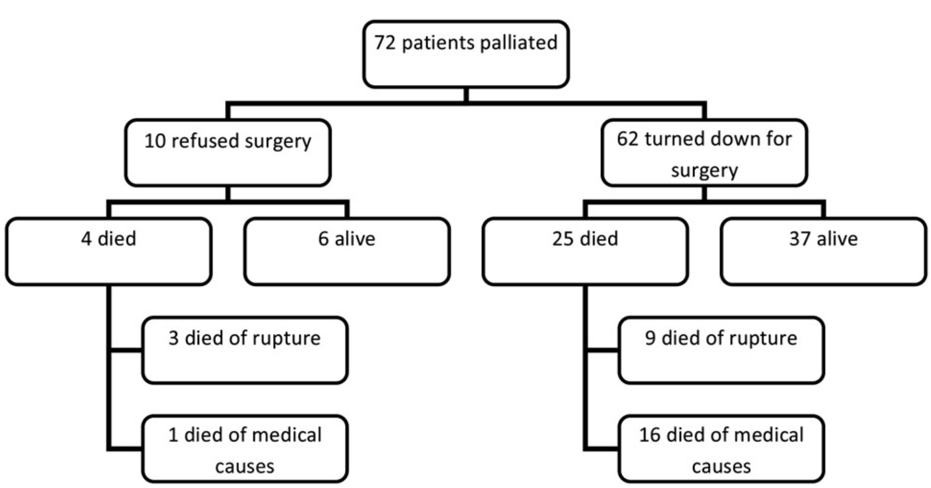


Figure 3. Flow-chart demonstrating outcomes of our patient cohort.

Table 2. Features of non-operated AAA when stratified according to size.

Aneurysm size	5.1–6.0 cm	6.1–7.0 cm	>7.0 cm
Number of patients	45	20	7
Median age (range, standard deviation)	79(58–93, SD 7.9)	83(67–91, SD 5.9)	84(75–94, SD 6.7)
Alive	29	12	2
Dead – rupture (%)	5 (11%)	4 (20%)	3 (43%)
Dead – non-rupture	11	4	2
Median survival: months (range)	44 (1.5–72)	26 (0.5–75)	6 (0.4–17)

elective repair due to age, comorbidities or patient refusal. Of this series 13% died intra-operatively from shock, 8% died in the first 5 days following surgery and a further 18% died between day 6 and 3 months. He argued that as 60% of this group who underwent emergency aneurysm repair survived to leave hospital, but elective mortality in this centre was less than 3%, "**all aneurysms should be treated pre-rupture, independent of comorbidities**".

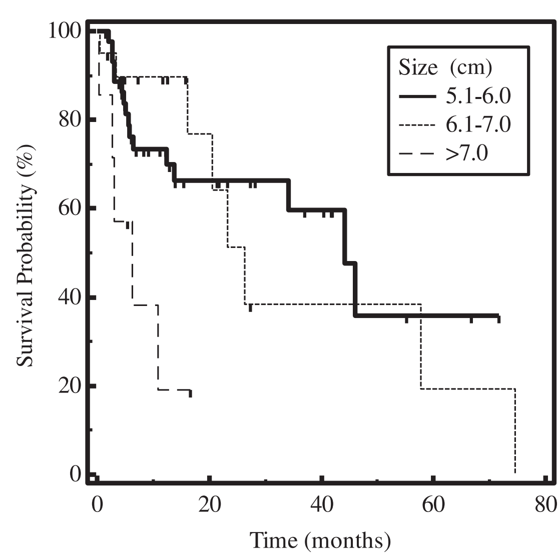
So, could we have improved survival in our study group by operating on all cases? 59% of deaths were due to causes other than rupture and 30-day mortality in the 4 patients who, subsequent to initial assessment, underwent repair was 50% indicating that an aggressive surgical approach in this cohort carries a high mortality and suggests that in the majority of cases, outcomes would be unchanged. However, it is not just quantity but quality of life which must be taken into account. A longer post-operative inpatient stay, with associated complications and the complex issues surrounding health care economics also need to be considered if long-term survival is not greatly improved in this cohort.

Median survival in those who died from aneurysm rupture was significantly greater than that for those who died of other medical causes (11 months vs. 5 months, $P = 0.04$). This reflects severity of comorbity and demonstrates the futility of operative intervention in the non-rupture cohort.

Cardio-pulmonary exercise testing is an accepted pre-operative investigation in elective major surgical cases as it offers a standardised, reproducible measure of physiological fitness. Armed with this information, clinicians can make an objective judgement regarding surgical suitability and patients themselves have a measure of their fitness and so how they may fare intraoperatively. The sensitivity of CPEX to predict survival following surgical intervention is well illustrated. A study by Older et al., looking at outcomes in the elderly following major intra-abdominal surgery, demonstrated a mortality of 18% in the group whose pre-op anaerobic threshold was <11, whereas in those with an anaerobic threshold >11 mortality was 0.8% ($P < 0.001$).[14]

56% of our cohort (40 patients) underwent CPEX assessment and on testing, only 4 of 40 patients achieved an anaerobic threshold greater than or equal to 11, the level generally taken as the cut off for cardiopulmonary capacity to withstand major surgery.[14] Of these 4 patients, 1 declined surgery, the other 3 had small abdominal aneurysms (<6 cm), 1 with a co-existent thoracic aneurysm.

Within our series, mortality in the CPEX group was significantly lower than that in those who did not undergo testing ($P < 0.05$). This reflects the fact that CPEX testing was, in the early stages, only employed in those borderline cases in which there was uncertainty (69% of patients of ASA grade 3 were tested, compared with 32% of ASA grade



Number at risk:

5.1 - 6.0cm	45	15	8	2	0
6.1 - 7.0cm	20	6	2	1	0
> 7.0cm	7	0	0	0	0

Figure 4. Survival when stratified according to aneurysm size.

Table 3. Comparison of studies in the literature assessing outcome of unfit patients with AAA.

Study authors	Date	Size of cohort	% Mortality	Rupture deaths as a % of all-cause deaths	Rupture deaths as a % of total cohort size
Szilagyi et al.[2]	1944—1965	223	78%	45%	35%
RC Darling[10]	1952—1968	282	Autopsy series	29%	29%
Conway et al.[11]	1989—1999	106	72%	49%	35%
Jones et al.[9]	1985—1994	57	88%	38%	33%
Brown et al.[12]	1976—2001	400	32%	31%	10%
Heikkinen et al.[6]	1990—1998	23	87%	25%	22%
Lederle et al.[8]	1995—2000	198	57%	40%	23%
Tambyraja et al.[13]	1995—1999	125	61%	36%	22%
Western et al.	2006—2009	72	40%	41%	17%

4), there being little clinical doubt in those not undergoing assessment about their inability to survive operative stress.

Also of note, 80% (4 out of 5) of patients with an ASA grade of 2 who did not undergo CPEX testing, declined operative repair.

There were 10 patients in our study who declined surgery. Median survival in this group was markedly longer than that in the group turned down for operation and this is unsurprising given that the majority of patients who refused operation were suitable candidates for surgery had they been in agreement with clinical recommendations.

Patients not suitable for operative AAA repair should of course be medically optimised to reduce both cardiovascular and rupture risk. Statin use has been shown to reduce both rupture risk and expansion rate,[15—17] as have ACE inhibitors[18] and there is an inverse correlation between cigarette smoking and aneurysm growth.[19] These measures are part of the standardised regime for optimisation of cardiovascular risk factors undertaken in all vascular patients.

Given the higher frequency of rupture in larger aneurysms, a more aggressive surgical approach is often taken and, in comorbid patients, operative intervention may be delayed until aneurysm size increases adequately to warrant operative risk. The balance between surgical risk and benefit is dynamic and may change as an AAA enlarges. The issue of palliation may therefore need to be revisited and this cohort may benefit therefore from continued aneurysm surveillance.

LIMITATIONS OF OUR STUDY

Cause of death in most cases was defined by death certificate and this is therefore a potential source of inaccuracy as deaths attributed to rupture, where no premortem CT scan or post-mortem were performed, cannot be verified. Another potential limitation arises from the radiological assessment of aneurysm size. Aneurysm size was defined in our unit as maximum diameter measurable, independent of orientation, rather than maximum antero-posterior diameter, which is thought to be more reproducible[20] and a better predictor of rupture risk.[21,22] In some individuals, CT alone was performed or was the most up to date imaging; a modality which often over-estimates AAA size when compared with ultrasound.[23,24] However, the adjustment of aneurysm diameter by a few millimetres at most is unlikely to have influenced decision making in most cases.

CONCLUSIONS

Even in the era of minimally invasive techniques, through greater understanding of the natural history of AAA and patient-related factors, risk stratification can be used to select those likely to benefit from prolonged life expectancy as a result of intervention. CPEX testing is used in our centre to assist decision making and by employing such a standardised multidisciplinary approach to patient selection nationwide through anaesthetic, surgical and radiological input we may reduce operative mortality. The potential to improve operative survival by pre-operative medical optimisation and physical conditioning is an area for future study.

ETHICS

As data was retrospectively analysed, no informed consent was obtained.

FUNDING

There was no funding source for this piece of research.

CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest in relation to this research.

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